High Spatial Resolution Cerebral Blood Flow Imaging of Rat Brain

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INTRODUCTION Cerebral blood flow (CBF) is an important physiological parameter. CBF is tightly regulated and intricately coupled to basal metabolic function under normal physiologic conditions. Perturbations of basal CBF have been implicated in many neurological diseases such as stroke, brain tumor, and neurodegeneration. The majority of CBF studies in rat brain are ~500x500x2000 microns using single shot EPI using either continuous arterial spin labeling (cASL) or dynamic susceptibility contrast techniques. The goal of this study is to image CBF of the rat brain at 75μm x 56μm x 1mm using cASL. By constructing a digital atlas, CBF of 146 structures and their tissue volumes were obtained automatically. This study sets the stage for investigating CBF dysfunction for a wide range of neurological diseases at very high spatial resolution.

METHODS Six male adult SD rats (250~300g) were anesthetized with ~1.2% isoflurane in air. Body temperature, respiration rate, heart rate and blood oxygen saturation level were continuously monitored and maintained within normal ranges. MRI experiments were performed on a Bruker 11.7T/16cm scanner. Quantitative CBF was measured using the two-coil cASL technique (1, 2) with four-shot, gradient-echo EPI. MRI parameters were: FOV = 19.2x14.4mm, matrix = 192x144 and reconstructed to 256x256, TR = 3s, TE = 9ms, labeling duration = 2.65s and post-labeling duration = 250ms. Fifteen 1mm slices were acquired in three separate blocks to cover the whole brain. Two hundred pairs of images were acquired in each scan (scan time = 80 mins).

A rat brain digital atlas was created by digitizing a PDF format rat brain atlas (3). Fifteen slices ranging from slice No.7 (interaural 12.70 mm) to slice No.65 (interaural -2.30 mm) were identified and used to co-register with CBF images. CBF and volume of 146 structures were analyzed. Some of these structures included cortex, caudate putamen, cerebellum, hippocampus, amygdale, thalamus, hypothalamus and corpus callosum. Large vessel pixels (CBF > 2ml/gram/min) were excluded from the quantitative analysis. All data were reported as mean ± SD and $p < 0.05$ was taken as statistical significance for paired t-test.

RESULTS **Figure 1** showed the quantitative CBF maps of a representative rat. Excellent CBF contrasts were observed among different cortical and sub-cortical structures. Descending arterioles in the cortices were apparent. Whole brain CBF was 0.89±0.16 ml/g/min.

Figure 2 showed the digital rat brain atlas overlaid on anatomy. The major structures were color-coded and presented, whereas the smaller structures are not color-coded. The cerebral cortex included the restrosplenial, limbic, singulate, motor, somatosensory, auditory, visual, insular, temporal association, perihinal, entorhinal and parietal association cortex. Similarly, other small structures were also grouped together by function and/or proximity for presentation. The group-averaged CBF values and their % volumes are summarized in **Table 1**. The CBF standard deviation of the structures presented ranged from 11-36% (with an average of 20%). The limbic, cingulated and entorhinal cortices showed slightly higher CBF among cortices. The motor and somatosensory cortices constituted about half of the total cortical volume and their CBF (0.91 ml/g/min) dominated the mean CBF value of cortex (0.92 ml/g/min). The cerebral cortices constituted about one fourth of whole brain volume. Compared with the cerebral cortex, the caudate putamen showed significant higher CBF. The cerebellum, hippocampus, amygdale, thalamus, hypothalamus and corpus callosum showed significantly lower CBF than cortical CBF. CBF of corpus callosum, cerebellum and hypothalamus were among the lowest.

DISCUSSION & CONCLUSION This study presents high spatial resolution CBF images of rat brain and, along with a digital atlas, CBF of 146 structures were derived. The standard deviations of the structures presented in Table 1were overall acceptable. Future studies will need to establish a method to determine CBF reliability of each structure. If CBF values of individual structures were unreliable, we need to determine how they should be grouped together (i.e., by proximity and function) to achieve adequate SNR. Other structures near the ear canals suffered from susceptibility artifacts due to the gradient echo EPI acquisition. Minimizing such susceptibility artifacts (i.e., by injecting susceptibility neutral gel into ear canals or use spin-echo acquisition) is needed. In conclusion, this study sets the stage for investigating CBF dysfunction for a wide range of neurological diseases at very high spatial resolution.

REFERENCE: 1) Duong TQ, et al., MRM 2000; 43: 338. 2) Silva AC, et al., JCBFM 2000; 20: 201. 3) Paxinos G & Watson C, The rat brain in stereotaxic coordinates, 1998.

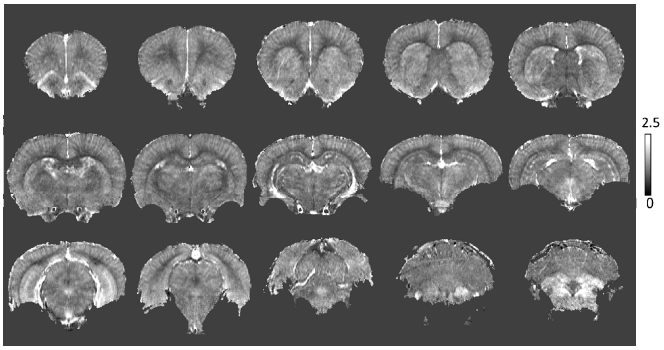

Figure 1 CBF maps (n=1). Scale bar unit = ml/g/min.

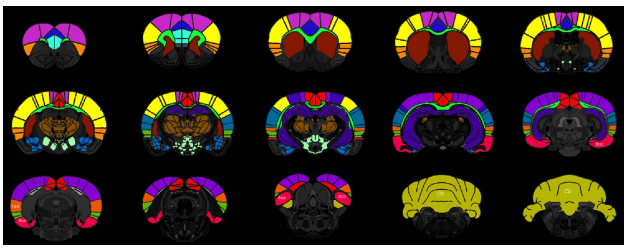

Figure 2 Digital rat brain atlas. Analyzed structures are color-coded.

Table 1 CBF and volume (% of whole brain) of different structures

structures		CBF (ml/g/min)		volume (%)	
cortex	retrosplenial	0.88±0.22	0.92 ±0.16	1.41±0.07	22.35 ±0.12
	limbic	1.05±0.14		0.46±0.07	
	cingulate	1.11±0.12		0.73±0.08	
	motor	0.91±0.13		3.26±0.10	
	somatosensory	0.91±0.14		6.97±0.13	
	auditory	0.90±0.17		1.37±0.17	
	visual	0.86±0.24		3.71±0.14	
	insular	0.95±0.19		1.37±0.18	
	temporal association	0.87±0.20		0.69±0.11	
	perirhinal	0.84±0.22		0.73±0.13	
	entorhinal	1.02±0.20		1.26±0.08	
	parietal association	0.98±0.19		0.39±0.18	
caudate putamen		1.10±0.15		5.09±0.10	
cerebellum		0.66±0.24		3.82±0.24	
hippocampus		0.79±0.13		1.97±0.06	
amygdala		0.75±0.21		0.37±0.10	
thalamus		0.83±0.16		1.26±0.12	
hypothalamus		0.72±0.13		0.44±0.15	
corpus callosum		0.31±0.04		3.34±0.05	